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09/015,078	01/29/98	SUERBAUM	S 2356-0073-01
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EXAMINER

TURNER, S

ART UNIT

PAPER NUMBER

1647

DATE MAILED:

01/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/015,078

Applicant(s)

Suerbaum

Examiner

Sharon L. Turner, Ph.D.

Group Art Unit

1647



☒ Responsive to communication(s) filed on 1-9-00

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

- ☒ Claim(s) 31-36 and 43-61 is/are pending in the application.
- Of the above, claim(s) 31-36, 45-46, 51-52, 57(b)-(e) is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 43-44, 47-50, 53-56, 57(a) and 58-61 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☒ Claims 31-36 and 43-61 are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of References Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1647

Response to Amendment

1. The Art Unit of U.S. Patent application SN 09/015,078 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1647.
2. The amendment filed 11-9-00 has been entered into the record and has been fully considered.
3. Claims 37-42 are canceled. Claims 31-36 and 43-61 are pending.
4. Applicants are reminded of the species election imposed in the original restriction requirement of 6-16-99 in which species a) a bacterial strain lacking the hook protein of *H. pylori* was elected for prosecution in the response of 8-16-99. The species as set forth were distinct because they differ in phenotypic characteristics, and thus the relevant searches are not co-extensive. Applicants have canceled all claims and chosen to present the invention in different terms. The amendment to the claims has separated specific species, necessitating withdrawal of such claims from examination as set forth below.

In addition, the amended claims now set forth a new invention. Whereas the claims previously were restricted to *H. pylori* mutants which are deleted or substituted in the *flbA* gene, instant claims include mutants which express *flbA* (without mutation by insertion, substitution or deletion) but which exhibit phenotypes of aflagellate *H. pylori* as recited in the claims, i.e., in which the *flbA* gene is expressed but such expression does not enable the A and B flagellins to be synthesized, 3) the *flbA* gene is expressed but such expression does not enable the sheath to

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be synthesized, 4) the flbA gene is expressed but such expression does not enable the anchoring protein to be synthesized, and 5) the flbA gene is expressed but such expression does not enable the hook protein to be synthesized, each phenotype constituting of different bacterial strains which are patentably distinct based on different phenotypic and genotypic characteristics. Thus, newly submitted claims 43-61 include inventions that are independent or distinct from the invention originally claimed.

Since applicant has received an action on the merits for the originally presented invention (flbA mutants) this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the subject matter of claims 43-61 as directed to such *H. pylori* mutants which express flbA (non flbA mutants) are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. The claims should be rewritten to exclude such subject matter. Failure to do so may result in the issuance of a non-responsive letter. The claims are, at present, limited to elected species a) *H. pylori* lacking the hook protein.

5. Claims 31-36, 45-46, 51-52, 57(b)-(e) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.
6. As a result of applicants amendment all rejections have been withdrawn by the examiner.
7. The following new grounds of rejection are set forth with respect to the new claims.

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Priority

8. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on July 4, 1995. It is noted, however, that applicant has not filed a certified translated copy of the 95 08068 application as required by 35 U.S.C. 119(b).

Rejections Necessitated by Amendment

Claim Objections

9. Claim 55 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 55 recites "the bacterial extract of an aflagellate strain of H. pylori", however this claim does not further limit claim 49 which is already drawn to an aflagellate strain.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 43-44, 47-50, 53-56, 57(a), and 58-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting antibodies in a patient sample, does not reasonably provide enablement for a method of in vitro detection of an infection due to H. pylori in a sample of biological fluid from a patient comprising the recited

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steps. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is newly applied in response to applicants arguments that the prior art of record cannot read over applicants invention because the patient rabbit was not infected with *H. pylori*. The examiner acknowledges this as the case. However, in light of applicants arguments it is apparent that the reference which meets the method steps of applicants claims, namely bringing a patient sample in contact with an *H. pylori* bacterial strain having an aflagellate phenotype (regardless of the strain) and detecting an immunological reaction between the bacterial strain and antibodies directed to *H. pylori* and which are present in the sample does not, as applicants point out detect infection. This may be due for example to the presence of cross-reactive epitopes or the persistence of antibody following a primary and secondary antigenic stimulus, termed the memory (anamnestic) response in the host which manifests as the presence of reactive antibodies in the absence of *H. pylori* infection, see in particular *Immunology: A short course*, Benjamini Ed., Wiley Liss, p. 174-75. Thus, while applicant may detect antibodies, such measurement as claimed is not indicative of *H. pylori* infection and therefore the skilled artisan cannot make and use the claimed invention. Arguments to the contrary which would imply that the method steps are what is essentially required to practice applicants invention would require the reinstatement of the previous art rejections in the absence of further clarification or delineation of the strains distinguishing characteristics which would exclude the art.

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In addition, the examiner notes that the claims appear to recite the following phenotypes; an aflagellate phenotype resulting from a mutation in the flbA gene of said *H. pylori* bacterial strain such that 1) the flbA gene is no longer expressed, 2) the flbA gene is expressed but such expression does not enable the A and B flagellins to be synthesized, 3) the flbA gene is expressed but such expression does not enable the sheath to be synthesized, 4) the flbA gene is expressed but such expression does not enable the anchoring protein to be synthesized, and 5) the flbA gene is expressed but such expression does not enable the hook protein to be synthesized. Yet, the specification does not appear to enable the artisan to make and use or specifically identify the aforementioned strains which differ in phenotypic and genotypic characteristics. For example, there is no guidance whereby one phenotypic strain is achieved over the other, there is no direction as to what directs a particular strain to exhibit or lack the hook protein. The skilled artisan recognizes the unpredictability in the art with respect to the prediction of phenotype based on the appearance of either similar or dissimilar genotypes, see in particular O'Toole of record, Haas of record and further Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. Thus, in view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue experimentation to make and use the claimed invention.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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13. Claims 43-44, 47-50, 53-56, 57(a), and 58-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants claims include transitional phrases including "either...or...or...", followed by "and" in addition to the phrase "if this is the case" and "and which" which phrases cannot readily be interpreted by the skilled artisan. Clarification and clear antecedent basis is required. For example, "present in the sample" may modify either the antibodies or the *H. pylori*.

14. Claims 43-44, 47-50, 53-56, 57(a), and 58-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is newly applied in light of applicants arguments that the previous art rejections of record fail to meet applicants limitations with respect to "the *flbA* gene", the "hook", "flagellins A and B" and newly applied as amended to the "anchoring protein", "sheath" in particular as it pertains to the aflagellate phenotype. The metes and bounds of the relevant phenotypic and genotypic characteristics of the bacterial strains cannot be readily discerned from the claims. For example, the previous art of record cites a *flaA* mutant which is aflagellate in phenotype and which lacks biosynthesis of A flagellin by mutagenesis. It is presumed that the *flbA* gene, if different from *flaA* is still expressed as it was not mutated, and that B flagellin is lacking as the reference notes that the strain lacks flagella (is aflagellate) and thus appears to inherently fall within the scope of the claim limitations, i.e., "or the expression of the *flbA* gene

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in the *H. pylori* bacterial strain does not enable the A and B flagellins" as recited. The prior art reference has been withdrawn in view of applicants arguments in regard to infection as set forth above, however amendment of the claims without clarification of the metes and bounds of the required phenotypic and genotypic constraints may necessitate reinstatement of the previous rejection.

Status of Claims

15. No claims are allowed.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
January 23, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud